Claims 1, 2, 11, 13, 16-23, 30, 34, and 41 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. More specifically, the Examiner objects to the formula recited in Claims 1 and 18 cites SEQ ID NOS: 37-39 as the corresponding sequences. Claim 1 has been amended to recite a different formula, C-3X-C-(10-12)X-C-3X-C, which does correspond to SEQ ID NOs: 37-39. Support for amended Claim 1 can be found in the Specification page 4, lines 26-27 and in original Claim 1. Claim 18 is dependant on amended Claim 1.

Claims 2 and 11 were amended as suggested by the Examiner. Claim 2 was amended to include the language "selected from the group consisting of:" and Claim 11 was amended to "of" instead of "according to".

Claim 13 is amended to recite that the word "controlling" means "reducing the number of" to show that effect of "controlling" is to reduce the number of.

Claim 16 is amended to more clearly recite the method.

Claim 19 is amended to recite sequence 29 to 94 of SEQ ID NO:24 and 1 to 23 of SEQ ID NO:26. Support for amended Claim 19 can be found in the Specification page 4, lines 15-17.

The rejection of Claim 22 is obviated by the amended sequence listing.

In view of the amendments to the Specification, figure legends, and sequence listing, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §103(a)

Claims 1-3, 11, 13, 16-23, 30, 34, and 41 are rejected under 35 U.S.C. §103(a) as being unpatentable over McHenry et al. (Plant Molecular Biology, vol. 18, pages 1173-1176, 1992) in view of Duvick et al. (U.S. Patent No. 5,905,187, May 17, 1995), and Spencer et al. (U.S. Patent No. 5,770,433, January 21, 1993).

Applicants would like to point out an error in the enclosed ALIGNMENTS. It appears that the Examiner has used the cocoa vicilin gene (SEQ ID NO:7 in this application) as the Query as well as the DB in RESULT I, page 1, column 2. The query sequence does not match any of the claimed sequences in Claim 2 (SEQ ID NOS:1, 3, and 5). In addition, Applicants would like to note that they are not claiming the full-length SEQ ID NOS: 23, 25, and 28 (Maize, Soybean, and S.sinuatus vicilin proteins). Applicants are only claiming **fragments** containing

the motif C-3X-C-(10-12)X-C-3X-C and the full-length proteins corresponding to SEQ ID NOS:1, 3, and 5.

In addition, Applicants would like to point out that the Sequence Alignments represent the following sequences in this Application: SEQ ID NOS: 7, 7, 8, 7, 7, 7, 7, 8, 23, 28,25,23,21,25,24,24,22,22,22, in that order as received. No alignments were provided for SEQ ID NOS: 1, 3, and 5 which represent the *M. integrifolia* vicilin proteins of the present invention. Therefore, there are no alignments which show that, as the Examiner states, "McHenry et al. teach the sequences contained in SEQ ID NOS:1, 3, and 31-39 of the present application with a high sequence identity (see the alignments)". In fact no such alignments are provided. Furthermore, Figure 6 of the present invention shows that SEQ ID NOS:1, 3, and 5 (corresponding to Mi clone 1, 2, and 3), in fact, have very different sequences from the cocoa vicilin protein identified in the McHenry et al. and Spencer et al. prior art. Additionally, although Duvick et al disclose a Maize protein which corresponds to SEQ ID NO:23 in the present application, applicants are not claiming SEQ ID NO:23, but only provide it in the sequence listing for comparison. Therefore, the prior art references do not teach or suggest the *M. integrifolia* proteins which correspond to SEQ ID NOS:1, 3, and 5.

Amended Claim 1 of the present invention, recites that the peptide **fragments** comprise a sequence with the relative spacing C-3X-C-**(10-12)**X-C-3X-C. None of the references teach a peptide **fragment** with antimicrobial activity and none of the references teach that such a fragment with the relative spacing C-3X-C-**(10-12)**X-C-3X-C will have antimicrobial activity. McHenry and Spencer teach only a full-length anti-microbial protein which has seed storage activity. Duvick et al. teaches an antimicrobial protein which has a relative spacing of C-3X-C-**(13)**X-C-3X-C. In addition, Duvick et al does not identify motif as necessary or involved in the anti-microbial activity.

As mentioned, Duvick et al. does disclose a polypeptide referred to in the patent as CMIII, which has antimicrobial properties. However, the CMIII polyeptide does not include the motifs of Claim 1 (see Example 2 and the sequence listing), but are spaced apart by thirteen amino acid residues. As mentioned in the present specification, page 14, line 29, to page 15, line 2, it is stated that:

"Although MiAMP2 subunits also share some homology with MBP-1 antimicrobial protein from maize (Duvick, J.P. et al. (1992) J Biol Chem 267:18814-20) the number of residues between the CXXXC motifs is 13 which puts MBP-1 outside the specifications for the spacing given here in the application."

Spencer et al. and McHenry et al. disclose a number of polypeptides but refer to their function only as seed storage proteins and does not suggest that they would be active as antimicrobial proteins in a truncated form. In fact, Spencer and McHenry do not even suggest or teach that the proteins would be active in any way in a truncated form or that they would have antimicrobial activity. They have no idea that there is any antimicrobial function. Therefore, the presently claimed invention is not obvious in view of McHenry et al., Duvick et al., and Spencer et al. because none of them teaches a truncated protein with the claimed motif which acts as an antimicrobial protein.

In addition, the three references do not teach all of the claimed elements, because the combined references do not teach a protein with the claimed motif which has antimicrobial activity. The present invention is an antimicrobial protein with at least one CXXC(**10-12X**)CXXC motif. In fact, the combination of references would teach away from the present invention because the combination of references teaches that the proteins which have a CXXXC **(13X)**CXXC motif can act as an antimicrobial protein, and those which do not have the 13 amino acid motif are seed storage proteins, since only the protein with 13 amino acids between the motifs has antimicrobial activity.

In summary, the combination of prior art references does not teach all of the elements of the claimed invention because they do not teach fragments with antimicrobial activity. Nor do they teach that the CXXC(10-12X)CXXXC motif is necessary and sufficient for antimicrobial activity. In fact, the claimed references teach that the protein must be full-length and possess a CXXC(13X)CXXC motif to possess antimicrobial activity. Therefore, in view of the above amendments and arguments, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103(a).

VERIFICATION UNDER 37 C.F.R.§1.821(f) & (g)

All of the sequences in the attached Sequence Listing were included in the application as filed. Pursuant to 37 C.F.R.§1.821(g), no new matter is being added herewith. As required

under 37 C.F.R.§1.821(f), I hereby verify that the data on the enclosed disk and the paper copies of the Sequence Listing are identical.

Conclusion

Should there be any questions concerning the above-captioned patent application, the Examiner is respectfully requested to contact the undersigned attorney at the number appearing below.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 8 Dec. 2000

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